

CLAIMS

1. A genetically modified *Bordetella* strain having a partial or complete loss of function in the endogenous *aroQ* gene and a lower capacity to propagate in a mammalian host but remaining viable in the host for a period of time sufficient to induce an immune response against a pathogenic *Bordetella* strain.
2. The genetically modified strain of claim 1, wherein the pathogenic *Bordetella* strain is a natural pathogenic *Bordetella* counterpart of the genetically modified *Bordetella* strain, or related organism.
3. The genetically modified strain of claim 1, wherein the pathogenic *Bordetella* strain is from *Bordetella avium*, *Bordetella bronchiseptica*, *Bordetella holmesii*, *Bordetella parapertussis* and *Bordetella pertussis*.
4. The genetically modified strain of claim 1, wherein the pathogenic *Bordetella* strain is *Bordetella pertussis*.
5. The genetically modified strain of claim 1, comprising a disruption in the endogenous *aroQ* gene.
6. The genetically modified strain of claim 5, wherein the disruption has been introduced into the genome of a pathogenic strain of *Bordetella* by homologous recombination with a DNA targeting construct such that the targeting construct is stably integrated in the genome, wherein the disruption of the *aroQ* gene results in a reduced level and/or functional activity of the 3-dehydroquinase.
7. The genetically modified strain of claim 5, comprising an exogenous nucleic acid sequence in its genome, or on an extrachromosomal element, which is capable of abolishing or otherwise reducing the expression of *aroQ* or the level and/or functional activity of the 3-dehydroquinase encoded by *aroQ*.
8. The genetically modified strain of claim 5, comprising an exogenous nucleic acid sequence in its genome, or on an extrachromosomal element, which is capable of abolishing or otherwise reducing the expression of *aroQ* or the level and/or functional activity of the 3-dehydroquinase encoded by *aroQ*, wherein the nucleic acid sequence comprises at least a portion of *aroQ*, in the sense or anti-sense orientation, which is operably linked to a transcriptional control element.

9. The genetically modified strain of claim 5, comprising an exogenous nucleic acid sequence in its genome, or on an extrachromosomal element, which is capable of abolishing or otherwise reducing the expression of *aroQ* or the level and/or functional activity of the 3-dehydroquinase encoded by *aroQ*, wherein the nucleic acid sequence comprises a ribozyme-encoding polynucleotide that is operably linked to a transcriptional control element, wherein the ribozyme specifically binds to or otherwise interacts with a transcript of the *aroQ* gene.
10. The genetically modified strain of claim 1, further having a partial or complete loss of function in at least one other endogenous gene selected from a *pur* gene, another *aro* gene, a pertussis toxin gene, or any other gene which contributes to survival in the host and/or to bacterial virulence, or a combination thereof.
11. The genetically modified strain of claim 1, wherein the *pur* gene is selected from *purA*, *purE* or *purH*.
12. The genetically modified strain of claim 1, wherein the *aro* gene is selected from *aroA*, *aroB*, *aroC* or *aroE*.
13. The genetically modified *Bordetella* strain of claim 1, comprising at least one exogenous gene which is capable of expressing an antigen that is heterologous or foreign to the *Bordetella* strain.
14. The genetically modified *Bordetella* strain of claim 13, wherein the heterologous or foreign antigen is derived from a pathogen that is unrelated to the *Bordetella* strain.
15. The genetically modified *Bordetella* strain of claim 13, wherein the heterologous or foreign antigen is derived from a pathogen that infects by the mucosal route.
16. An isolated polynucleotide comprising a nucleotide sequence that corresponds or is complementary to at least a portion of the sequence set forth in SEQ ID NO: 1 or 3.
17. The polynucleotide of claim 16, wherein the nucleotide sequence has at least 70% sequence identity to at least a portion of the sequence set forth in SEQ ID NO: 1 or 3.
18. The polynucleotide of claim 16, wherein the nucleotide sequence is capable of hybridising to at least a portion of the sequence set forth in SEQ ID NO: 1 or 3 under at least medium stringency conditions.
19. The polynucleotide of claim 16, wherein the portion is at least 18 nucleotides in length.

20. The polynucleotide of claim 16, wherein the portion is a biologically active fragment of the sequence set forth in SEQ ID NO: 1 or 3.
21. An isolated polypeptide comprising an amino acid sequence that corresponds to at least a portion of the sequence set forth in SEQ ID NO: 2.
22. The polypeptide of claim 21, wherein the amino acid sequence has at least 70% sequence identity to at least a portion of the sequence set forth in SEQ ID NO: 2.
23. The polypeptide of claim 21, wherein the portion is at least 6 amino acids in length.
24. The polypeptide of claim 21, wherein the portion is a biologically active fragment of the sequence set forth in SEQ ID NO: 2.
25. A nucleic acid construct for disrupting an *aroQ* gene in a *Bordetella* cell, comprising:
a) a non-homologous replacement portion; b) a first homology region located upstream of the non-homologous replacement portion, the first homology region having a nucleotide sequence with substantial identity to a first *aroQ* gene sequence; and c) a second homology region located downstream of the non-homologous replacement portion, the second homology region having a nucleotide sequence with substantial identity to a second *aroQ* gene sequence, the second *aroQ* gene sequence having a location downstream of the first *aroQ* gene sequence in a naturally occurring endogenous *aroQ* gene of the *Bordetella* cell.
26. The construct of claim 25, wherein the *aroQ* gene comprises the sequence set forth in SEQ ID NO: 1 or 3 or a variant or derivative thereof.
27. A vector comprising a nucleotide sequence that corresponds or is complementary to at least a portion of the sequence set forth in SEQ ID NO: 1 or 3.
28. The vector of claim 27, wherein the vector is a DNA targeting vector.
29. A host cell containing the construct of claim 25 or the vector of claim 27.
30. An antigen-binding molecule that is specifically interactive with the polypeptide of claim 21.
31. A method for producing a genetically modified *Bordetella* strain, comprising introducing the nucleic acid construct of claim 25 into a *Bordetella* cell under conditions such that the nucleic acid construct is homologously recombined into the *aroQ* gene in the

genome of that cell to produce a genetically modified *Bordetella* cell containing a disrupted *aroQ* gene.

32. The method of claim 31, wherein the genetically modified *Bordetella* cell containing the homologously recombined nucleic acid construct is further characterised by expressing reduced or undetectable levels of *aroQ*.

33. The method of claim 31, wherein the genetically modified *Bordetella* cell lacks the ability to produce a functional 3-dehydroquinase encoded by said *aroQ* gene.

34. A composition, comprising the genetically modified *Bordetella* strain of claim 1, together with a pharmaceutically acceptable carrier.

35. The composition of claim 34, further comprising an adjuvant.

36. A composition of matter comprising dendritic cells which have been exposed to the genetically modified *Bordetella* strain of claim 1 for a time and under conditions sufficient to express a processed or modified antigen derived from the *Bordetella* strain for presentation to, and modulation of, T cells.

37. The composition of matter of claim 36, which is in the form of an *in vitro* cell culture.

38. A method for modulating an immune response, comprising administering to a patient in need of such treatment an effective amount of the genetically modified *Bordetella* strain of claim 1, or the composition of claim 34 or the composition of matter of claim 36.

39. A method for the treatment and/or prophylaxis of whooping cough or related condition, comprising administering to a patient in need of such treatment an effective amount of the genetically modified *Bordetella* strain of claim 1, or the composition of claim 34 or the composition of matter of claim 36.

40. Use of the genetically modified *Bordetella* strain of claim 1 in the study, and modulation of an immune response.

41. The use of claim 40, wherein the immune response is against a pathogenic strain of *Bordetella* or related organism.